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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,164	04/09/2001	Katsuhiko Nakata	01130/HG	6458

1933 7590 10/03/2003

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EXAMINER	
AUDET, MAURY A	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 10/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/787,164	NAKATA ET AL.	
	Examin r	Art Unit	
	Maury Audet	1654	

-- The MAILING DATE of this communication app ars on the cover sh t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, and 4-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Joshi et al. (US 5252318) or Hoeg et al. (US 5434133).

The claimed invention is drawn to eyedrops for promoting lacrimal secretion (claim 1) or treating a keratoconjunctival disorder (claim 2) containing a natriuretic peptide as an active ingredient in an ophthalmic vehicle (claims 1-2); and a method of treating a person having a keratoconjunctival disorder (such as dry eye (claim 5), corneal erosion (claim 6), or corneal ulcer (claim 7)) comprising administering an effective amount of a natriuretic peptide (such as atrial (ANP; claim 8), brain (BNP; claim 9), or C-type (CNP; claim 10)) to at least one eye (claim 4).

Joshi et al. teach eyedrops (col. 9, lines 50-55) to increase lacrimal fluid (col. 9, lines 34-44; col. 12, lines 63-68; col. 17, lines 2-24; col.) and treat keratoconjunctivitis (i.e. dry eye; col. 10, lines 61-62), using an effective amount of a natriuretic peptide (i.e. ANP, col. 12, lines 14-15).

Claims 1-2, and 4-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Joshi et al. (US 5252318) or Hoeg et al. (US 5434133).

Hoeg et al. teach eyedrops (col. 12, lines 61-67) to increase lacrimal fluid (col. 12, lines 47-57; col. 16, lines 14-20; col. 22, lines 62-68 and col. 23, lines 1-15; claims 3 and 25) and treat keratoconjunctivitis (i.e. dry eye; col. 14, lines 5-6), using an effective amount of a natriuretic peptide (i.e. ANP, col. 15, lines 33-34).

> [Background Note: ANP (or cardiodilatin) is naturally present in the cells of the lachrymal glands and plays a physiological role controlling sodium transport and secretion, lachrymal secretion is characterized by a certain sodium content and there secretion activation system which controls the steady flow sodium lachrymal secretion, and the cardiodilatin-containing cell system in the lachrymal glands contributes to the control of homeostasis during lachrymal secretion. (See Lange et al. (Exp. Eye Res., 50, 1990, 313-316), also discussed below under 35 U.S.C. § 103). "Cardiodilatin is a peptide of the class of natriuretic peptides. These peptides play an important role in regulating the balance of salts and water in the body. The prototype of natriuretic hormones is cardiodilatin, also referred to in literature as atrial natriuretic peptide (CDD/ANP). [ ] Instead of the designation cardiodilatin, the literature frequently uses the designation "atrial natriuretic peptide" (ANP)" (See Immer et al., US 5767239; col. 1, lines 50-54, and col. 2, lines 6-9)].

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, and 4-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Joshi et al. (US 5252318) or Hoeg et al. (US 5441732), in view of Tanaka et al. (US 434133) and Haidt (US 4452818).

Joshi et al. and Hoeg et al. are discussed above. Joshi et al. and Hoeg et al. both teach eyedrops to increase lacrimal fluid and treat keratoconjunctivitis (i.e. dry eye), using an effective amount of a natriuretic peptide (i.e. ANP). Joshi et al. and Hoeg et al. do not expressly teach that the eyedrops may be used for all disorders classified as keratoconjunctivitis (i.e. corneal erosion,

corneal ulcer) or that all possible natriuretic peptides (i.e. BNP, CNP) may be used in the eyedrops.

Tanaka et al. teach that many "natriuretic peptides" or "NPs":

> "having different chain lengths or similar primary amino acid sequences have heretofore been isolated and identified from living bodies and it has *now become clear that all of those NPs are biosynthesized from three different NP precursor proteins (prepro ANP, prepro BNP and prepro CNP)*" (col. 1, lines 20-26). It was also verified that both *ANP and BNP, when administered in vivo, exhibited comparable* and noticeable levels of natriuretic and hypotensive actions. On the basis of those findings, both ANP and BNP are presently considered to work not only as hormones to be secreted from the heart into blood but also as nerve transmitting factors, thereby playing an important role in maintaining the homeostatic balance of body fluid volume and blood pressure (col. 44-53). The primary *amino acid sequence of CNP is similar to those of ANP and BNP and, when administered in vivo, CNP exhibits natriuretic and hypotensive actions. Therefore, CNP has been held assignable to the NP family*" (col. 2, lines 31-35).

Haidt teaches eyedrops for lacrimal deficiency as "[a] topical agent which would provide lubrication and protection to the external surfaces of the eye is required in these disorders. Such disorders include dry eyes syndrome caused by keratoconjunctivitis sica, tear abnormalities, atrophy of the lacrimal gland, ocular pemphigoid, chemical burns, chronic keratoconjunctivitis, corneal epithelium diseases (corneal ulcers, recurrent corneal erosion and marginal ulcers), and corneal vascularization due to corneal injury, infection or transplantation (abstract; col. 1, lines 26-35; col. 7, lines 51-59).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use any natriuretic peptide (including BNP and CNP) for any keratoconjunctivitis condition (including corneal erosion/ulcer; increasing lacrimal fluid therefor), in the eyedrops of either Joshi et al. or Hoeg et al., because Tanaka et al. teach that BNP and CNP are peptides closely related to ANP, and classified in the same peptide family (natriuretics) and Haidt teaches that keratoconjunctivitis is a general class of conditions (which

also includes corneal ulcer/erosion) where lacrimal secretion (the underlying etiology) is deficient, and since Joshi et al. and Hoeg et al. already teach the use of ANP (of which, as discussed in the background above, Immer et al. teach that ANP or cardiodilatin, is the prototype of natriuretics) for keratoconjunctivitis (dry eye).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 1-2, and 4-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lange et al. (Exp. Eye Res., 50, 1990, 313-316), in view of EP 385476 (Daiichi Pure Chemicals Co.) or EP 466174 (Hisayuki Matsuo) and JP 10-218792 (Santen Pharmaceutical Co.) or JP 10-236972 (Mitsubishi Chemical Corp.).

Lange et al. teach that the natriuretic peptide cardiodilatin is present the cells of the lachrymal glands, that it plays a physiological role controlling sodium transport and secretion, that lachrymal secretion is characterized by a certain sodium content and there secretion activation system which controls the steady flow sodium lachrymal secretion, and that the cardiodilatin-containing cell system in the lachrymal glands contributes to the control of homeostasis during lachrymal secretion (abstract, discussion). [Background Note: See Immer et al. (US 5767239; col. 1, lines 50-54, and col. 2, lines 6-9), discussed above under 35 U.S.C. § 102, as to cardiodilatin being synonymous with ANP]. Lange et al. does not teach use of

ANP/cardiodilatin in eye drops, or in a method for promoting lachrymal secretion or treating keratoconjunctivitis (i.e. dry eye, corneal erosion/ulcer).

EP 385476 and EP 466174 (and many other references in the prior art) teach use of natriuretic peptides generally.

JP 10-218792 and JP 10-236972 (and many other references in the prior art) teach eye drops and methods of using which act on the lachrymal glands to promote lachrymal secretion when lachrymal secretion is inadequate (see claims and paragraphs 0002 and 0008 and claims and paragraphs 0002 and 0006; respectively).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use any natriuretic peptide (including BNP and CNP) for any keratoconjunctivitis condition (i.e. to increase lacrimal fluid in dry eye, corneal erosion/ulcer), in an eyedrop composition based on Lange et al., because either EP 385476 or EP 466174 teach the advantageous general use of natriuretic peptides (such as ANP, BNP, or CNP) and because either JP 10-218792 or JP 10-236972 teach the use of eye drops to increase lacrimal fluid; since Lange et al. teach that ANP is already known to be present in lacrimal fluid and it is generally known that deficient lacrimal secretion is a symptom of keratoconjunctivitis conditions (i.e. dry eye, corneal erosion/ulcer)

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at

the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 703-305-5039. The examiner can normally be reached from 7:00 AM – 5:30 PM, off Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached at 703-306-3220. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-1234 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

MA
September 28, 2003

CHRISTOPHER R. TATE
PRIMARY EXAMINER